Quick reference guideline for monitoring of disease modifying anti-rheumatic drug (DMARD) therapy

View the BSR and BHPR guideline: Disease-modifying anti-rheumatic drug (DMARD) therapy for further information

<table>
<thead>
<tr>
<th>DRUG</th>
<th>TYPICAL DOSE</th>
<th>PRE-TREATMENT</th>
<th>FBC</th>
<th>U&amp;E, Creat (1)</th>
<th>LFT</th>
<th>BP</th>
<th>URINE DipStick protein</th>
<th>FREQUENCY / COMMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azathioprine</td>
<td>1mg/kg/day increase at 4-6 weekly intervals to max 3mg/kg/d</td>
<td>FBC, U&amp;E, LFT, Creatinine, TPMT assay (See main text)</td>
<td>√</td>
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<td>√</td>
<td>_</td>
<td>_</td>
<td>FBC and LFT weekly for 6 weeks and then every 2 weeks until dose stable for 6 weeks; then monthly.</td>
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<tr>
<td>Ciclosporin</td>
<td>Start 2.5mg/kg/day in two divided doses for 6 weeks and then may be incrementally increased by 25mg at 2-4 weekly intervals until clinically effective or the maximum dose of 4mg/kg is reached</td>
<td>FBC, U&amp;E, LFTCreatinine: Twice at 2 week apart – to obtain mean value Creatinine clearance or equivalent Fasting Lipids BP: ≤140/90 on 2 occasions at 2/52 apart.</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>_</td>
<td>_</td>
<td>U &amp; E including potassium and Creatinine every 2 wks until dose and results stable for 3 months and then monthly FBC and LFT monthly until dose and results stable for 3 months; thereafter 3 monthly. Vigilance when NSAID added particularly diclofenac- reduce diclofenac dose by 50% Blood pressure monitoring each attendance. BP &gt; 140/90 on 2 consecutive readings 2/52 apart – treat hypertension before stopping ciclosporin (Note possible drug interactions). If BP cannot controlled, stop ciclosporin and obtain BP control before restarting ciclosporin Check fasting lipids periodically</td>
</tr>
<tr>
<td>I / M Gold (Myocrisin)</td>
<td>Test dose 10mg then 50mg weekly until a total dose 1000mg is given when efficacy should be reviewed.</td>
<td>FBC, U &amp; E, LFT &amp; Creatinine, Urinalysis</td>
<td>√</td>
<td>_</td>
<td>_</td>
<td>_</td>
<td>_</td>
<td>FBC and urinalysis at time of each injection. Provided blood results are stable, the results of the FBC need not be available before the injection is given but must be available before the next injection i.e. it is permissible to work one FBC in arrears. Urinalysis must be done before each injection Ask each time about presence of skin rash or mouth ulcers</td>
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| Hydroxychloroquine | 200-400mg daily. Max 6.5mg/kg/day                 | FBC, U&E, LFT Ask about visual impairment not corrected by glasses. Record near visual acuity of each eye (with reading glasses if worn) using a test type or reading chart If abnormality detected refer first to an optometrist |     |                |     |    |                        | Annual review either by an optometrist or enquiring about visual symptoms, rechecking visual acuity and assessing for blurred vision using the reading chart. Discuss with ophthalmologist if on treatment for >5 years
 Patients should also be advised to report any visual disturbance                                                                                                                                                                                                                      |
| Leflunomide    | 10mg – 20mg daily. Maximum 20mg daily when monotherapy is used. Advised to use 10mg daily in combination with other hepatotoxic drugs such as methotrexate | FBC, U&E, LFT, Creatinine. Blood Pressure on 2 occasions 2 weeks apart. If >140/90 treat before starting Rx Body weight. | √   |     | √   |    |                        | FBC, LFT every month for 6 months and, if stable, 2 monthly thereafter. If co-prescribed with another immunosuppressant or potential hepatotoxic agent then blood checks should be continued long-term, at least once a month.
 ALT/AST 2-3x upper limit normal – reduce dose to 10mg, recheck weekly. If normalised – continue 10mg; if remains elevated withdraw drug and discuss with specialist team.
 If ALT/AST >3x normal, stop drug, recheck within 72 hours. If still >3x, withdraw drug and consider washout.
 BP each visit. If BP >140/90 treat in line with NICE guidance. If BP remains uncontrolled, stop leflunomide and consider washout.
 Weigh at each visit. If >10% weight loss with no other cause identified, reduce dose or stop and consider washout.                                                                                                                                                                  |
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| Methotrexate (2)      | 7.5 - 25 mg ONCE a week. Increase every 2-6 weeks to maximum dose of 25mg ONCE weekly. Rarely max 30mg/week  
(See main text)  
5 mg ONCE weekly  
≥24 hours after Methotrexate | 1. FBC, U&E, LFT, CXR (within the last 6 months) & 2. Pulmonary Function Test in selected patients. | √   | √             | √   | _  | _                      | FBC, U&E, LFT every 2 weeks until dose and monitoring stable for 6 weeks; thereafter monthly, until the dose and disease is stable for a year. Thereafter based on clinical judgement and following discussion with specialist team consider reducing frequency of monitoring to every 2 - 3 months (see main text)  
Albumin – unexplained fall (in absence of active disease) – withhold and discuss  
New or increasing dyspnoea or dry cough – withhold and discuss urgently with the specialist team  
Avoid prescribing trimethoprim or cotrimoxazole to patients receiving methotrexate – greatly increases risk of marrow aplasia  
For discussion of use of pro-collagen III see main text |
| Folic Acid            | 5 mg ONCE weekly ≥24 hours after Methotrexate                                  | FBC, U&E, LFT & CXR (within the last 6 months)                                | √   | _             | _   | _  | _                      | FBC weekly until dose stable for 4 weeks then fortnightly for 2 months.  
Monthly thereafter, even after patient is stabilized on treatment. |
| Mycophenolate Mofetil | Start 500mg daily increase weekly by 500mg to optimal or max. tolerated dose. Max - 3 gms /day | FBC, U&E, LFT & CXR (within the last 6 months)                                | √   | _             | _   | _  | _                      | FBC and urinalysis every 2 weeks until dose and monitoring stable for 3 months; monthly thereafter.  
Ask about skin rash or oral ulceration at every visit |
| D-Penicillamine       | Start 125-250mg/day increase by 125 mg, 4 weekly initially to 500mg. Max dose 750mg/day (see main text) | FBC, U&E, Creatinine & Urinary Protein                                       | √   | _             | _   | _  | √                      |                                                                                                           |
| Sulfasalazine         | Start at 500mg/day increasing by 500mg each weekly to maximum of 2.0–3.0 gm/day. May occasionally go above 3 gms/ day (See main text) | FBC, U&E, LFT, Creatinine                                                   | √   | _             | √   | _  | _                      | FBC, LFT monthly for 3 months. If dose and bloods stable for 3 months, then 3 monthly. If dose increase, repeat bloods one month after dose increase; if stable revert to usual monitoring regime. If after first year dose and blood results stable, frequency of blood tests can be reduced to every 6 months for second year of treatment. After 2 years of therapy, blood monitoring can be discontinued.  
Ask about skin rash or oral ulceration |
Please note that in addition to absolute values for haematological indices a rapid fall or rise and a consistent upward or downward trend in any value should prompt caution and extra vigilance.

(1) U/E and creatinine, CRP and ESR / PV should be checked every 6 months – this will enable monitoring of renal disease and disease activity

(2) IM/SC Methotrexate conforms to the same protocol for monitoring as oral Methotrexate.

1. **General advice**
   - This is a summary of the most relevant monitoring requirements. Refer to full text of guideline for further information. [http://www.rheumatology.org.uk/resources/guidelines](http://www.rheumatology.org.uk/resources/guidelines)
   - The summary guideline does not address combination therapy – read full text of guideline for advice
   - Beware drug interactions
   - Review individual monitoring protocols when dose changes are implemented.
   - Patients should not receive immunisation with live vaccines
   - Beware infections treat vigorously - check FBC and U & E
   - Beware oral ulceration/sore throats/nosebleeds/bruising/rash
   - If patients come into close contact with Herpes Zoster, consider passive immunisation
   - If blood pressure >140/90 manage hypertension according to NICE Hypertension Guidance

2. **Consult table for test and frequency**
   - Any discretionary reduction in the frequency of monitoring should only be on the instruction of a Rheumatology specialist
   - Enter result in patient-held record book

3. **Withhold treatment & liaise with Specialist team in charge of patient's treatment if:-**
   - Severe rash or bruising or ulceration of mucous membranes.
   - Any unexplained illness occurs including nausea or diarrhoea
   - WCC falls <3.5 x 10^9/l
   - Neutrophils <2.0 x 10^9/l
   - Eosinophils >0.5 x 10^9/l
   - Platelet count falls below <150 x 10^9/l
   - MCV > 105 f/l
   - Creatinine >30% of baseline
   - LFTs (ALT or AST) increase > 2 fold rise above upper limit reference range (Leflunomde special rules – see above and full text)
   - If urinary protein on dipstick is 2+ send a MSU for culture. If MSU confirms infection, treat appropriately. If sterile proteinuria – seek advice.